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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,787	06/26/2001	Carl Nelson Skold		4399

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EXAMINER	
DO, PENSEE T	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,787	SKOLD, CARL NELSON	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-56 and 58-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *77* is/are allowed.

6)☒ Claim(s) *73* is/are rejected.

7)☒ Claim(s) *54-56,58-72 and 74-76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/06/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S80

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 6, 2005 has been entered.

Claims 54-56, 58-77 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 75 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 75 recites "the coupling agent" which lacks antecedent basis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 54-56, 58-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson (US 4,672,040) in view of Bradbury et al. (US 5,855,790).

Josephson teaches a method of separating a target material from a liquid mixture, comprising: forming and at least purifying aggregates of two or more crystallites of a magnetizable metal oxide; coating the formed and at least purified aggregates with a polymer such as silane to form coated aggregates and treating the coated aggregates so that the polymer of silane has a binding affinity for the target material to form treated aggregates; combining the treated aggregates with the liquid mixture containing the target material for a sufficient time for the target material to bind to the polymer of silane; applying a magnetic field to the combination and separating the treated aggregates, including the target material bound thereto, from the liquid mixture, using the magnetic field. The magnetic particles comprise a magnetic metal oxide core surrounded by an adsorptively or covalently bound silane coat to which a wide variety of bioaffinity adsorbents can be covalently bonded through selected coupling chemistries. The method for preparing the magnetic particles comprises precipitating metal salts in base to form fine magnetic metal oxide crystals. (see col. 9, line 27-col. 13). The target material is an organic material, an organic compound or a biological material such as antibodies, antigens, nucleic acid, etc. The crystallites have a particle size of greater than 500 Angstrom if they are ferromagnetism. The treated aggregates have diameter between 0.1 and 1.5 microns (equivalent to 100 nm – 1500 nm). The magnetizable metal oxide is a magnetizable iron oxide (see col. 12, lines 5-63). The aggregates are formed by a step of treating precipitated magnetite with a base to form a colloidal

suspension. The precipitate is washed with sodium chloride solution. (see col. 12, lines 29-33). The treated aggregates are combined with the sample mixture by being dispersed or suspended in a reactor. The aggregates are coated by bonding an organosilane directly to the aggregate of crystallites of the magnetizable metal oxide and bonding the polysaccharide material to the organosilane. (see col. 17, line 50-col. 18, line 25; table III). Bioaffinity adsorbent such as a ligand couples to the organosilane coating of the metal oxide cores by their organofunctionalities. (see col. 7, line 67-col. 8, line 9).

However, Josephson fails to teach the coating is a polysaccharide, coating the aggregates includes steps of bonding the polysaccharide material directly to the aggregate of crystallites of the magnetizable metal oxide;

Bradbury teaches magnetic particles, which comprise a core of a magnetic material, surrounded by a mixture of fibrous material and a solid binding agent. The core consists of particles of iron oxide or other magnetic material. The fibrous material comprises an organic polymer in the form of fibers such as cellulose. Cellulose is a polysaccharide. (see col. 2, lines 43-61; example 2).

It would have been obvious to one of ordinary skills in the art to coat a polysaccharide on the magnetic particles as taught by Bradbury and use in the method of Josephson since both teach the same method of preparing the magnetic particles coated with a polymer. Polymers have the function of protecting the magnetic particles from attack by the aqueous solution. They also contain specific function groups, which are specifically intended to absorb selectively a particular ligand that binds to a

substance of interest. With the polymer coating around the magnetic particles, the ligand can be attached to the magnetic particles through the functional groups of the polymer.

Claims 54-56, 58-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson (US 4,672,040) in view of Kito et al.

Josephson has been discussed above.

However, Josephson fails to teach the coating is a polysaccharide, coating the aggregates includes steps of bonding the polysaccharide material directly to the aggregate of crystallites of the magnetizable metal oxide; and a step of aging the crystallites; a step of attaching the polysaccharide material to a pendant functional group on the organosilane; attaching the affinity to the polysaccharide via the functional group; pendant functional group is carboxyl group, a carbonate, an amino group, an aldehyde group, or a sulfuryl group; polysaccharide is a dextran.

Kito teaches a composition containing magnetic metal oxide ultra fine particles, which exist in crystal, form and comprises an aqueous sol of complex of the magnetic metal oxide ultra fine particles with a polysaccharide, a polysaccharide derivative and/or a protein; and an organic monocarboxylic acid. The magnetic metal oxide ultrafine particles are prepared by: an alkali coprecipitation method, an ion exchange resin method. The alkali coprecipitation method comprises mixing aqueous solution containing divalent metal salt and a trivalent metal salt preferably an iron salt with a base such as NaOH, KOH or NH4OH; if necessary heating and aging; after separation and water washing of the magnetic metal oxide precipitated, redispersing the magnetic

metal oxide in water, and adding a mineral acid such as a hydrochloric acid to obtain a magnetic metal oxide aqueous sol. If necessary, these aqueous sols can be purified and/or concentrated by dialysis, ultrafiltration and centrifugation, etc. The magnetic metal oxide aqueous sol and a polysaccharide and/or protein aqueous solution were mixed to coat the polysaccharide on the magnetic metal oxide (see col. 3, lines 50-col. 4, line 25; col. 8, lines 20-35). The polysaccharide is a dextran. The diameter of the particles is 10 to 500 nm. (see col. 8, lines 57-62). The polysaccharide is a carboxyl polysaccharide, which contains a pendant carboxyl group. (col. 3, line 44). The metal salts can be salts with mineral acids such as hydrochloric acid, sulfuric acid, and nitric acid. (see col. 5, lines 23-25).

It would have been obvious to one of ordinary skills in the art to use the idea of coating the polysaccharide as taught by Kito on the magnetic particles such as those in the method of Josephson since both teach coating a polymer on magnetic metal oxide. Coating the polysaccharide on the magnetic particles provides specific functional group that attaches a ligand/binder, which in turn couples to a substance of interest for use in assays. Regarding claim 68, since Josephson teaches that the organosilane couples to the affinity/coupling group via function groups and Kito teaches that polysaccharide has a pendant group, it would have been obvious to one of ordinary skills in the art to couple the affinity/coupling group via the functional group of either the polysaccharide or the organosilane.

Claims 54-56, 58-69, 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson in view of Miltenyi (US 6,417,011).

Josephson has been discussed above.

However, Josephson fails to teach the coating is a polysaccharide, coating aggregates includes the steps of bonding the polysaccharide material directly to the aggregate of crystallites of the magnetization metal oxide; dissociating the treated aggregates and target material after the separation step so that they no longer bound together and removing the treated aggregates by a magnetic field; pendant group is carboxyl, amino acid or sulfhydryl; the polysaccharide is dextran; the specific binding member is a protein, nucleic acid, antibody.

Miltenyi teaches a method of magnetic gradient separation using a magnetic support comprising preparing the superparamagnetic particles by reacting ferric and ferrous salts to form magnetic oxide particles which form aggregates. These aggregates are then removed by means of filtration or centrifugation and the magnetic aggregates are coated with a coating of polysaccharide such as dextran. (see col. 7, lines 45-67). These coated magnetic particles can bind to a specific binding moiety, which is directed to a target biological material, the polysaccharide is suitably derivatized to provide functional groups such as aldehyde functional groups, for conjugation to specific binding moiety. The specific binding agents are antibody, nucleic acids, enzyme, ligand or binding proteins (see col. 8, line 53-col. 9, line 16). Miltenyi further teaches an elution step of target analytes after separation of the unbound by removing the magnetic field. (see col. 11, lines 50-65). The aggregates are treated with ammonium hydroxide before coating. The bonding of polysaccharide is directly to the aggregate. The aggregates are dispersed in a liquid mixture.

It would have been obvious to one of ordinary skills in the art to coat the polysaccharide directly on the aggregates of magnetic particles as taught by Miltenyi for use in the method of Josephson since both teach the same method of preparing the magnetic particles coated with a polymer. Polymers have the function of protecting the magnetic particles from attack by the aqueous solution. They also contain specific function groups, which are specifically intended to absorb selectively a particular ligand that binds to a substance of interest. With the polymer coating around the magnetic particles, the ligand can be attached to the magnetic particles through the functional groups of the polymer. Miltenyi teaches that the polysaccharide can be directly linked to the aggregates of magnetic oxides and such polysaccharide also has binding affinity for a specific binding member. Thus, one of ordinary skills in the art would have reasonable expectation of success in directly linking the polysaccharide to the aggregates.

Claims 70-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Josephson and Miltenyi as applied to claims 54-56, 58, 59, 61-69, 74-76 above, and further in view of Niswender (US 4.048,298).

Josephson and Miltenyi have been discussed above.

However, Josephson and Miltenyi fail to teach that the pendant group of the polysaccharide is a carboxyl group attached to the polysaccharide through a linker having at least one heteroatom to every three carbon atoms in the linker; the heteroatom of the linker is oxygen; and the linker is derived from ethylene glycol, an oligoethylene glycol or a polyethylene glycol.

Niswender teaches a polymeric carrier with a suitable reactive group. The reactive groups are carboxyl, hydroxyl and primary or secondary amine groups. The polymeric material is polysaccharides, dextran. The reactive group can be crosslinked by inclusion of a substantial amount of a polyethylenically unsaturated monomer, such as ethylene glycol dimethacrylate.(see col. 4, lines 5-45).

It would have been obvious to one of ordinary skills in the art to attach carboxyl group to polysaccharide via an ethylene glycol linker as taught by Niswender to form a polymeric coating on the magnetizable particles of Josephson and Miltenyi since these polymeric coatings are used for attaching ligands/antibody to detect target analyte in assay.

Response to Arguments

Applicant's arguments filed on September 06, 2005 have been fully considered but they are not persuasive.

Regarding the rejection of Josephson in view of Bradbury, Applicants argue that Josephson fails to teach polysaccharide having specific binding member having affinity for the target and that Bradburry discloses coating magnetite having particles sizes between 7 and 12 microns which are too large and that Josephson teaches away from large particles by disclosing that "mean diameter in solution greater than 10 microns can respond to weak magnetic fields and gradients; tend to settle rapidly, have a more limited surface area per weight then smaller particles, so that less material can be coupled to them". Applicants conclude that it would not be obvious to combine those two references.

Although Josephson teaches that polysaccharide reacts with target analyte in solution, it is not necessary that polysaccharide equates to the specific binding member. Polysaccharides have affinity groups or functional groups that bind covalently with the functional group on a target substance. Thus, the affinity group can be interpreted as a specific binding member having binding affinity to the target. Thus, Josephson is still applicable to such limitation of the present invention. Regarding the large size particles disclosed by Bradbury, such size does not completely fall in the range of "large size" (larger than 10 microns) disclosed by Josephson. The particles size of Bradbury can be less than 10 microns and thus would not associate with any of the problems discussed by Josephson. Therefore, one of ordinary skills in the art would find it obvious to combine these two references.

Regarding the 103 rejection over Josephson in view of Kito, Applicants argue that Josephson and Kito fail to teach coating the polysaccharide on the magnetic particles with a specific binding member and that Kito discloses coating magnetic particles with a polysaccharide, the polysaccharide is not used to attach specific binding member for target material or to directly bind a target material directly. Further, Applicants also argue that Kito does not discuss the carboxyl group.

As for the polysaccharide coated with specific binding member having affinity for the target analyte in Josephson, see discussion on Josephson above.

Kito does not have to discuss the carboxyl group. As long as Kito discloses a carboxyl group on a polysaccharide, such disclosure satisfies the requirement of the present invention.

Regarding claims 70-72, since the deficiency in Josephson is cured, rejection by Josephson in view of Kito and Niswender is still applicable. No further discussion is necessary.

Allowable Subject Matter

Claim 73 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

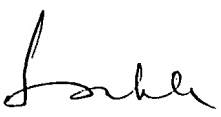
The prior arts fail to teach introducing the pedant functional group to the polysaccharide by reaction with chloroethoxyethoxyacetic acid and base.

Claim 77 is allowed over the prior arts. Claim 77 is an independent form of claim 73.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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10/03/05